AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-96 (Cancelled).

Claim 97 (Previously Presented): A signal amplification system comprising a bacterial multi-hybrid system of at least two chimeric polypeptides, comprising:

(a) a first chimeric polypeptide comprising a first fragment of a *Bordetella* adenylate cyclase catalytic domain and a molecule of interest fused to the first fragment; and

(b) a second chimeric polypeptide comprising a second fragment of the *Bordetella* adenylate cyclase catalytic domain and a target ligand fused to the second fragment;

wherein, when activity of the *Bordetella* adenylate cyclase is restored by *in vivo* interaction between the molecule of interest and the target ligand, a cAMP-mediated signal amplification is generated; and

wherein the signal amplification is performed in *E. coli* strain **BTH101** having C.N.C.M. Deposit Accession No. I-2309 or *E. coli* strain **DHM1** having C.N.C.M. Deposit Accession No. I-2310.

Claim 98 (Previously Presented): A signal amplification system comprising a bacterial multi-hybrid system of at least two chimeric polypeptides, comprising:

(a) a first chimeric polypeptide comprising a first fragment of the catalytic domain located within the first 400 amino acids of the *Bordetella pertussis* adenylate cyclase (CyaA) and a molecule of interest fused to the first fragment; and

(b) a second chimeric polypeptide comprising a second fragment of the catalytic domain located within the first 400 amino acids of the *Bordetella pertussis* adenylate cyclase (CyaA) and a target ligand fused to the second fragment;

wherein, when activity of the *Bordetella pertussis* adenylate cyclase (CyaA) is restored by *in vivo* interaction between the molecule of interest and the target ligand, a cAMP-mediated signal amplification is generated; and

wherein the signal amplification is performed in *E. coli* strain **BTH101** having C.N.C.M. Deposit Accession No. I-2309 or *E. coli* strain **DHM1** having C.N.C.M. Deposit Accession No. I-2310.

Claim 99 (Cancelled).

Claim 100 (Previously Presented): The signal amplification system according to claim 98, wherein the first and the second fragments of the catalytic domain of the *Bordetella pertussis* adenylate cyclase (CyaA) *in vitro* functionally interact with calmodulin (CaM), or a fragment thereof by restoring the activity of the catalytic domain of the *Bordetella pertussis* adenylate cyclase (CyaA).

Claim 101 (Previously Presented): The signal amplification system according to claim 100, wherein the first and the second fragments of the catalytic domain of the *Bordetella pertussis* adenylate cyclase (CyaA) are selected from:

(a) a fragment T25 corresponding to amino acids 1 to 224 of CyaA and a fragment T18 corresponding to amino acids 225 to 399 of CyaA;

(b) a fragment T25 corresponding to amino acids 1 to 224 of CyaA and a fragment corresponding to amino acids 224 to 384 of CyaA;

(c) a fragment corresponding to amino acids 1 to 137 of CyaA and a fragment corresponding to amino acids 138 to 400 of CyaA; and

(d) a fragment corresponding to amino acids 1 to 317 of CyaA and a fragment corresponding to amino acids 318 to 400 of CyaA.

Claim 102 (Previously Presented): The signal amplification system according to claim 101, wherein the first and the second fragments of the catalytic domain of the *Bordetella pertussis* adenylate cyclase (CyaA) are a fragment T25 corresponding to amino acids 1 to 224 of CyaA and a fragment T18 corresponding to amino acids 225 to 399 of CyaA.

Claim 103 (Previously Presented): The signal amplification system according to claim 101, wherein the first and the second fragments of the catalytic domain of the *Bordetella pertussis* adenylate cyclase (CyaA) are a fragment T25 corresponding to amino acids 1 to 224 of CyaA and a fragment corresponding to amino acids 224 to 384 of CyaA.

Claim 104 (Previously Presented): The signal amplification system according to claim 101, wherein the first and the second fragments of the catalytic domain of the *Bordetella pertussis* adenylate cyclase (CyaA) are a fragment corresponding to amino acids 1 to 137 of CyaA and a fragment corresponding to amino acids 138 to 400 of CyaA.

Claim 105 (Previously Presented): The signal amplification system according to claim 101, wherein the first and the second fragments of the catalytic domain of the *Bordetella pertussis* adenylate cyclase (CyaA) are a fragment corresponding to amino acids 1 to 317 of CyaA and a fragment corresponding to amino acids 318 to 400 of CyaA.

Claims 106-118 (Cancelled).

Claim 119 (Withdrawn): A method of selecting a molecule of interest capable of binding to a target ligand, comprising detecting an interaction between the molecule of interest and the target ligand with a signal amplification system according to claim 100, by means of generating a cAMP signal and triggering transcriptional activation or repression of a cAMP regulated reporter gene.

Claim 120 (Withdrawn): The method of selecting a molecule of interest according to claim 119, wherein the target ligand is selected from the group consisting

of protein, peptide, polypeptide, receptor, ligand, antigen, antibody, DNA binding protein, glycoprotein, lipoprotein, and recombinant protein.

Claim 121 (Withdrawn): The method of selecting a molecule of interest according to claim 119, wherein the amplification is quantified by measuring the level of cAMP generated.

Claim 122 (Withdrawn): The method of selecting a molecule of interest according to claim 119, wherein the amplification is quantified by measuring the expression of the reporter gene.

Claim 123 (Currently Amended): The method of selecting a molecule of interest according to claim 119, wherein the cAMP regulated reporter gene is selected from the group consisting of a gene coding for a nutritional marker, ~~such as lactose or maltose;~~ a gene conferring resistance to an antibiotic ~~antibiotics, such as ampicillin, kanamycin or tetracyclin;~~, a gene coding for a toxin;, a gene coding for ~~a color marker, such as the~~ Green Fluorescent Protein (GFP) ~~-~~;, a gene coding for a phage receptor protein, ~~or fragment thereof, such as~~ a gene coding for phage λ receptor, ~~or~~ and a gene coding for *lamb*, ~~or any gene encoding a gene product that confers a selectable phenotype~~.

Claim 124 (Withdrawn-Currently Amended): The method of selecting a molecule of interest according to claim 119, wherein the molecule of interest is a mutant

molecule compared to a known wild type molecule and the molecule of interest is tested for its capacity ~~of interacting~~ to interact with the target ligand.

Claim 125 (Withdrawn): A method of screening for a substance that stimulates or inhibits the interaction between a target ligand and a molecule of interest, comprising:

detecting the stimulating or inhibiting activity with a signal amplification system according to claim 100, by generating a cAMP signal in the signal amplification system to trigger transcriptional activation or repression of a cAMP regulated reporter gene;

measuring the expression of the reporter gene in the absence of the substance to be screened;

applying the substance to be screened to the signal amplification system;

measuring the expression of the reporter gene in the presence of the substance to be screened; and

comparing the level of expression of the reporter gene in the presence of the substance to be screened to the level of expression of the reporter gene in the absence of the substance to be screened;

wherein the substance to be screened is identified as a substance that stimulates the interaction between a target ligand and a molecule of interest if the level of expression of the reporter gene in the presence of the substance to be screened is higher than the level of expression of the reporter gene in the absence of the substance to be screened;

wherein the substance to be screened is identified as a substance that inhibits the interaction between a target ligand and a molecule of interest if the level of

expression of the reporter gene in the presence of the substance to be screened is lower than the level of expression of the reporter gene in the absence of the substance to be screened.

Claim 126 (Withdrawn): The method of claim 125, wherein the method is used to screen for a substance that stimulates the interaction between a target ligand and a molecule of interest.

Claim 127 (Withdrawn): The method of claim 125, wherein the method is used to screen for a substance that inhibits the interaction between a target ligand and a molecule of interest.

Claim 128 (Withdrawn): The method of screening for a substance that stimulates or inhibits the interaction between a target ligand and a molecule of interest of claim 125, wherein the target ligand is selected from the group consisting of protein, peptide, polypeptide, receptor, ligand, antigen, antibody, DNA binding protein, glycoprotein, lipoprotein, and recombinant protein.

Claim 129 (Currently Amended): The method of claim 125 of screening for a substance that stimulates or inhibits the interaction between a target ligand and a molecule of interest ~~of claim 125~~, wherein the cAMP regulated reporter gene is selected from the group consisting of a gene coding for a nutritional marker, ~~such as lactose or maltose;~~ a gene conferring resistance to an antibiotic ~~antibiotics, such as ampicillin,~~

~~kanamycin or tetracyclin;~~, a gene coding for a toxin~~;~~, a gene coding for ~~a color marker, such as the~~ Green Fluorescent Protein (GFP)~~;~~, a gene coding for a phage receptor protein, ~~or fragment thereof, such as~~ a gene coding for phage λ receptor, ~~or~~ and a gene coding for *lamb*~~, or any gene encoding a gene product that confers a selectable phenotype~~.

Claim 130 (Withdrawn): A method of selecting a molecule of interest capable of binding to a target ligand, comprising detecting an interaction between the molecule of interest and the target ligand with a signal amplification system according to claim 101, by means of generating a cAMP signal and triggering transcriptional activation or repression of a cAMP regulated reporter gene.

Claim 131 (Withdrawn): The method of selecting a molecule of interest according to claim 130, wherein the target ligand is selected from the group consisting of protein, peptide, polypeptide, receptor, ligand, antigen, antibody, DNA binding protein, glycoprotein, lipoprotein, and recombinant protein.

Claim 132 (Withdrawn): The method of selecting a molecule of interest according to claim 130, wherein the amplification is quantified by measuring the level of cAMP generated.

Claim 133 (Withdrawn): The method of selecting a molecule of interest according to claim 130, wherein the amplification is quantified by measuring the expression of the reporter gene.

Claim 134 (Currently Amended): The method of selecting a molecule of interest according to claim 130, wherein the cAMP regulated reporter gene is selected from the group consisting of a gene coding for a nutritional marker, ~~such as lactose or maltose;~~ a gene conferring resistance to an antibiotic ~~antibiotics, such as ampicillin, kanamycin or tetracyclin;~~, a gene coding for a toxin;, a gene coding for ~~a color marker, such as the~~ Green Fluorescent Protein (GFP)~~;~~, a gene coding for a phage receptor protein, ~~or fragment thereof, such as~~ a gene coding for phage λ receptor, ~~or~~ and a gene coding for *lamb*, ~~or any gene encoding a gene product that confers a selectable phenotype~~.

Claim 135 (Withdrawn-Currently Amended): The method of selecting a molecule of interest according to claim 130, wherein the molecule of interest is a mutant molecule compared to a known wild type molecule and the molecule of interest is tested for its capacity ~~of interacting~~ to interact with the target ligand.

Claim 136 (Withdrawn): A method of screening for a substance that stimulates or inhibits the interaction between a target ligand and a molecule of interest, comprising:

detecting the stimulating or inhibiting activity with a signal amplification system according to claim 101, by generating a cAMP signal in the signal amplification system to trigger transcriptional activation or repression of a cAMP regulated reporter gene;

measuring the expression of the reporter gene in the absence of the substance to be screened;

applying the substance to be screened to the signal amplification system;

measuring the expression of the reporter gene in the presence of the substance to be screened; and

comparing the level of expression of the reporter gene in the presence of the substance to be screened to the level of expression of the reporter gene in the absence of the substance to be screened;

wherein the substance to be screened is identified as a substance that stimulates the interaction between a target ligand and a molecule of interest if the level of expression of the reporter gene in the presence of the substance to be screened is higher than the level of expression of the reporter gene in the absence of the substance to be screened;

wherein the substance to be screened is identified as a substance that inhibits the interaction between a target ligand and a molecule of interest if the level of expression of the reporter gene in the presence of the substance to be screened is lower than the level of expression of the reporter gene in the absence of the substance to be screened.

Claim 137 (Withdrawn): The method of claim 136, wherein the method is used to screen for a substance that stimulates the interaction between a target ligand and a molecule of interest.

Claim 138 (Withdrawn): The method of claim 136, wherein the method is used to screen for a substance that inhibits the interaction between a target ligand and a molecule of interest.

Claim 139 (Withdrawn): The method of screening for a substance that stimulates or inhibits the interaction between a target ligand and a molecule of interest of claim 136, wherein the target ligand is selected from the group consisting of protein, peptide, polypeptide, receptor, ligand, antigen, antibody, DNA binding protein, glycoprotein, lipoprotein, and recombinant protein.

Claim 140 (Currently Amended): The method of screening for a substance that stimulates or inhibits the interaction between a target ligand and a molecule of interest of claim 136, wherein the cAMP regulated reporter gene is selected from the group consisting of a gene coding for a nutritional marker, ~~such as lactose or maltose;~~ a gene conferring resistance to an antibiotic ~~antibiotics, such as ampicillin, kanamycin or tetracyclin;~~, a gene coding for a toxin~~;~~, a gene coding for ~~a color marker, such as the~~ Green Fluorescent Protein (GFP)~~;~~, a gene coding for a phage receptor protein, ~~or fragment thereof, such as~~ a gene coding for phage λ receptor, ~~or~~ and a gene coding for *lamb*, ~~or any gene encoding a gene product that confers a selectable phenotype~~.

Claims 141 and 142 (Cancelled).

Claim 143 (Withdrawn): The method of selecting a molecule of interest according to claim 123, wherein the nutritional marker is lactose or maltose; the antibiotic is ampicillin, kanamycin or tetracyclin; the color marker is Green Fluorescent Protein (GFP); and the phage receptor protein is phage λ receptor or *lamb*.

Claim 144 (Withdrawn): The method of screening for a substance that stimulates or inhibits the interaction between a target ligand and a molecule of interest of claim 129, wherein the nutritional marker is lactose or maltose; the antibiotic is ampicillin, kanamycin or tetracyclin; the color marker is Green Fluorescent Protein (GFP); and the phage receptor protein is phage λ receptor or *lamb*.

Claim 145 (Withdrawn): The method of selecting a molecule of interest according to claim 134, wherein the nutritional marker is lactose or maltose; the antibiotic is ampicillin, kanamycin or tetracyclin; the color marker is Green Fluorescent Protein (GFP); and the phage receptor protein is phage λ receptor or *lamb*.

Claim 146 (Withdrawn): The method of screening for a substance that stimulates or inhibits the interaction between a target ligand and a molecule of interest of claim 140, wherein the nutritional marker is lactose or maltose; the antibiotic is ampicillin, kanamycin or tetracyclin; the color marker is Green Fluorescent Protein (GFP); and the phage receptor protein is phage λ receptor or *lamb*.